Respiratory Medicine CME 3 (2010) 85–86

Contents lists available at ScienceDirect

Respiratory Medicine CME

journal homepage: www.elsevier.com/locate/rmedc

Case Report

Fixed drug eruption: Aztreonam and ceftazidime cross-reactivity in cystic fibrosis, a case report

Hywel L. Cooper [a,*], Chris Pickard [a], Henry Marshall [b], Mary Carroll [b], Peter S. Friedmann [a]

[a] Dermatopharmacology Unit, University of Southampton, Southampton, UK
[b] Southampton University Hospital Trust, Southampton, UK

ARTICLE INFO

Article history:
Received 26 April 2009
Accepted 14 May 2009

Keywords:
Fixed drug eruption
Drug hypersensitivity
Cystic fibrosis
Ceftazidime
Aztreonam
Drug provocation

ABSTRACT

Fixed drug eruption is a manifestation of T-cell mediated drug hypersensitivity. We report, clinically confirm and highlight the occurrence of a fixed drug eruption with cross-reactivity between structurally related, though distinctly classified, antibiotics frequently used in the treatment of cystic fibrosis.

1. Letter

A 30-year-old man with cystic fibrosis developed painful, circular, oedematous, dusky red to violaceous dermal plaques over his back, finger webs, dorsal feet, thighs and volar aspect of wrist (Fig. 1A). This had been occurring in a progressively painful but erratic manner over 3 years. The lesions occurred in fixed positions within 1 h of receiving intravenous antibiotics for infective exacerbations of cystic fibrosis. Fixed drug eruption (FDE) was diagnosed. He had received multiple intravenous and oral combinations of penicillin (amoxicillin and flucloxacillin), cephalosporin (ceftazidime), monobactam (aztreonam), carbapenem (meropenem), aminoglycoside (tobramycin, gentamicin), polymyxin (colomycin), sulphonamide (septrin) and macrolide (erythromycin and clarythromycin) antibiotics as well as regular nebulised colomycin and tobramycin. Careful course by course evaluation suggested merepenem, gentamicin, aztreonam and ceftazidime to be the most likely causative agents.

Investigation with epicutaneous patch testing (0–30% drug mixed in Vaseline® within aluminium chamber applied to non-affected skin and eruption sites), and in-vitro lymphocyte transformation testing (isolated monocyte and lymphocyte cultures with increasing concentrations of suspected drug in-vitro) were non-diagnostic and drug provocation testing was performed. This demonstrated rapid reactivation of painful fixed plaques to aztreonam and ceftazidime within 30 min (Fig. 1B,C). Meropenem and gentamicin were without reaction and subsequently used at full clinical doses.

FDE was first described by Brocq in 1894.[1] It is characterised by the rapid onset of single or multiple circular erythematous to violaceous oedematous plaques on the skin though morphological variants have been described. These lesions maybe asymptomatic or painful, classically itching or burning. The pathognomic feature is the reappearance of the lesions at identical sites on re-exposure to the causative agent. Residual hyperpigmentation from lichenoid epidermal basal layer degeneration is characteristic. Histology of active lesions demonstrates marked oedema and a mixed perivascular infiltrate in the upper papillary.[2]

Immunological studies demonstrate a stable population of effector $CD8^+$ lymphocytes in resting lesions that are activated on administration of the causative drug resulting in localised damage. Viral infection has been suggested in the evolution of effector T-cells.[3] Familial clusters may hint at a genetic susceptibility.[4]

Confirmation of FDE by epicutaneous patch testing has been reported for certain drugs, whereas the in-vitro lymphocyte transformation test is unhelpful as drug specific lymphocytes are only found in the skin, not the peripheral circulation[5,6] Systemic provocation remains the gold standard.[4]

* Correspondence to: Hywel L. Cooper, Dermatopharmacology Unit, Southampton General Hospital, Mail point 825, Tremona Road, Southampton, SO16 6YD, UK. Tel.: +44 2380798975; fax. +44 2380706143.
E-mail address: hywel1@soton.ac.uk (H.L. Cooper).

1755-0017/$36.00 © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.rmedc.2009.05.008

Fig. 1. Cutaneous eruption seen subsequent to; A – clinically administered course of ceftazidime, gentamicin and flucloxacillin. B – administration of ceftazidime alone. C – administration of aztreonam alone.

Aztreonam, an antipseudomonal monobactam, lacks the bicyclic β-Lactam core structure characteristic of penicillins, cephalosporins and carbapenems but does share a common R-group side chain with ceftazidime. This means it has potential for cross-reactivity with ceftazidime but very little with penicillins, carbapenems or other cephalosporins.[7]

Antibiotic hypersensitivity is more prevalent in patients with cystic fibrosis, occurring in approximately one third, often to multiple drugs and correlates to cumulative drug exposure.[8] It is a clinically significant problem as these patients rely on prolonged and repeated courses of antibiotics to treat their chronic pulmonary sepsis and hypersensitivity reduces therapeutic choice. Clinical studies in cystic fibrosis patients support *in-vitro* studies with low levels of hypersensitivity to aztreonam even in penicillin-allergic patients.[9,10]

Although aztreonam–ceftazidime IgE mediated cross-reactivity is well known, to our knowledge, this is the first report of FDE to aztreonam–ceftazidime.

Conflict of interest

All authors declare they have no conflicts of interest.

Funding

Dr Hywel Cooper clinical research fellowship was supported by a Southampton University Hospitals Trust research and development grant. No additional funding.

Ethics statement

Ethical approval by Southampton and South West Local research ethics committee (REC ref 334/03/w) – "Investigation of the mechanisms underlying the development of adverse drug reactions".

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